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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/170,042	10/13/1998	GREGG HASTINGS	PF226D1	6370

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EXAMINER
HAYES, ROBERT CLINTON

ART UNIT	PAPER NUMBER
1647	14

DATE MAILED: 10/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/170,042	Hastings et al
Examiner	**Art Unit**
Robert C. Hayes, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *21-61* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *21-27, 34, and 36-61* is/are rejected.

7) ☒ Claim(s) *28-33 and 35* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Allowable Subject Matter

1. Claims 28-33 & 35 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 U.S.C. § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-47, 54-57 & 60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No proper antecedent nor conception in context of that described in the specification at the time of filing Applicants' invention is apparent for the broader concept of random epitope-bearing portions comprising "from about 75 to about 100/ about 168 to about 180/ about 204 to about 226/ about 258 to about 281/ about 291 to about 327 of SEQ ID NO:2" (i.e., as it relates to claims 38-42). In contrast to Applicants' assertions on page 7 of the first preliminary amendment, page 21 of the specification only contemplates specific "epitope- bearing portions"

consisting of these amino acid position numbers; thereby, constituting new matter. Likewise, no proper antecedent basis nor conception is apparent for the broader concept of "comprising at least 10 contiguous amino acids of SEQ ID NO:2" (i.e., as it relates to claims 43-47). In contrast to Applicants' assertions on page 8 of the preliminary amendment, no basis exists on pages 10, 13, 19 nor 21 of the specification; thereby, constituting new matter.

No proper antecedent nor conception in context of that described in the specification at the time of filing Applicants' invention is apparent for the broader concept of any polypeptide "fused to" any "heterologous polypeptide". In contrast to Applicants' assertions on page 8 of the preliminary amendment, pages 7 and 18 of the specification alternatively contemplate only fusion with polypeptides sequences that "aid in expression and secretion of the polypeptide", or aid in purification of the polypeptides of the instant invention; thereby, constituting new matter.

3. Claims 21-27, 34 & 36-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification describes the sole human polypeptide of SEQ ID NO:2. No other NAF-1 polypeptides are described from any other species. Accordingly, page 5 of the specification states that "NAF-1 does not appear to be the human counterpart of the rat FSP." In other words, no adequate written description of what constitutes any different species, allelic

variant (i.e., as both encompassed by the recitation of "at least 95%), or different open reading frame that merely "comprise" fragments of SEQ ID NO:2, or that "comprise" generic heterologous polypeptides fused to random fragments of SEQ ID NO:2 is provided within the instant specification, or known in the art. In addition, the specification fails to describe what critical amino acids define any distinguishable and assayable NAF-1 function/activity or what critical amino acid residues define functional "epitope-bearing portions" of SEQ ID NO:2. Nor could one skilled in the art reasonably visualize what constitutes such generic heterologous proteins encompassed by these claims, as currently and broadly claimed; thereby, not meeting the written description requirements under 35 U.S.C. 112, first paragraph.

Applicant is directed toward the Revised Interim Utility and Written Description Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999.

4. Claims 21-27, 34 & 36-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific polypeptide depicted as SEQ ID NO:2, does not reasonably provide enablement for any biological functional equivalent polypeptides/ fragments with little structural characterization and no distinguishable recited functional characteristics. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification describes the polypeptide of SEQ ID NO: 2 as having the functional activity of promoting neural cell adhesion and promoting axonal neurite extension (e.g., see page 10 of the specification). However, the name "polypeptide comprising" or "heterologous polypeptide" or "polypeptides comprising an amino acid sequence which is at least 95% identical..." does not sufficiently characterize and enable the polypeptides that are encompassed by these claims, because the inclusion of any random mutations or additional amino acid residues to truncated polypeptides with no known or disclosed function sets forth little structural characterization and no functional characteristics. In particular, the specification does not teach which particular amino acids are critical for any NAF-1 protein's function, nor how to distinguish such from any different polypeptide sequence that possesses none of the desired functions of the instant invention. Moreover, random mutations and/or random truncated variants of different NAF-1 -related polypeptides would be expected by the skilled artisan to result in generation of inactive proteins. For example, Rudinger states on page 3 that "it is impossible to attach a unique significance to any residue in a sequence. A given amino acid will not by any means have the same significance in different peptide sequences, or even in different positions of the same sequence". Rudinger further states on page 6 that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study". Therefore, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for any NAF-1 protein's function or pharmaceutical compositions thereof, or that are

necessary for successfully generating an antibody to such, would prevent the skilled artisan from determining whether any random mutation, modification or truncation to the specific amino acid sequence of SEQ ID NO: 2 could be made which retains the desired function of the instant invention, because any random mutation, truncation or modification, especially with additional random heterologous amino acid sequences manifested within such polypeptides would be predicted to adversely alter its biologically active 3-dimensional conformation, without requiring undue experimentation to determine otherwise.

5. Claims 50-53, 57 & 61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Only hybridization to the "fully complementary strand" of a polynucleotide would possibly produce a NAF-1 polypeptide encoded from the sense strand; thereby, being indefinite (i.e., as it relates to claim 50).

6. Claims 58-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is ambiguous how polypeptides merely comprising "epitope-bearing portions", or that merely "bind to an antibody specific to a polypeptide" can be used in a pharmaceutical

composition, or how a polypeptide merely comprising "at least 10 contiguous amino acids" or merely comprising other fragments of SEQ ID NO:2 with no recited functional requirements related to a pharmaceutical use are to be used in a pharmaceutical composition.

Claim Rejections - 35 U.S.C. § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 36, 50-53, 55, 57, 59 & 61 are rejected under 35 U.S.C. 102(b) as being anticipated by Jessell et al. (U.S. Patent 5,279,966).

Jessell et al teach rat F-spondin of SEQ ID NO:10 (e.g., cols. 8 & 35-40) that "comprises at least 7 contiguous amino acids of SEQ ID NO:2 fused/attached to the remaining heterologous amino acids of F-spondin (i.e., residue #s 188-194 of SEQ ID NO:2; as it relates to claims 7, 55 & 57). In that Jessell's polypeptide is encoded by a polynucleotide that would inherently hybridize under stringent conditions to residue # 580-599 of SEQ ID NO:1, and because Jessell's polypeptide possesses axonal neurite extension/outgrowth, neural adhesion and antibody binding activity (i.e., cols. 8-9, 12-14 & 16-20), and because Jessell et al. disclose pharmaceutical compositions of their protein, the limitations of claims 50-53, 57, 59 & 61 are also met.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
September 29, 2002

GARY KUNZ
SUPERVISORY PATENT EXAMINER
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